Declaration under 37 CFR §1.132	Attorney Docket No.	**3032-101**
	First Named Inventor	Igor Stagljar
	Title: **Method and kit for detecting membrane protein-protein interactions**	
	Application Number	10/509,507
	371(c) Date	December 22, 2004
	Group Art Unit	1636
	Examiner Name	Michele K. Joike

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Igor Stagljar, hereby declare and state:

THAT I am a citizen of Croatia;

THAT I have received the degree of Ph.D. in Molecular Biology from the Swiss Federal School of Technology (ETH) in Zürich, Switzerland;

THAT I am currently a professor at the Donnelly Center for Cellular and Biomolecular Research at the University of Toronto;

THAT I am also a co-founder and the Vice President of Dualsystems Biotech, Schlieren, Switzerland, the assignee of the entire interest in and to the subject application.

I further declare and state as follows:

I am one of the inventors of the invention described and claimed in the above-identified application.

I am also one of the co-authors of Stagljar et al (PNAS 95:5187-5192, 1998), the

primary reference applied by the Office in the Action of February 4, 2010.

I am familiar with the above-identified application. In relation thereto I have reviewed the Office Action mailed February 4, 2010, in which claims 48-55, 57-62 and 64-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stagljar et al (PNAS 95:5187-5192, 1998, specifically pp. 5187, 5191 and figure 2; hereinafter "Stagljar") in view of US 2005/0277116 (McKeon et al.) and US 6,251,676 (Shioda et al.).

In my opinion, one of ordinary skill in the art reading Stagljar at the time of the present invention would not have considered modifying Stagljar to maintain pRS305 (Δwbp1-Cub-PLV) episomally because an episomal expression of Stagljar's pRS305 (Δwbp1-Cub-PLV) would be expected to result in two types of Wbp1 proteins that would be expected to compete in the assay of Stagljar and thus would be expected to reduce its sensitivity.

My opinion is based on the following rationale:

Assuming that pRS305 (Δwbp1-Cub-PLV) would be maintained episomally, and would NOT be integrated, e.g., at the single *SpeI* site into the WBP1 gene as described in Stagljar (see page 5189, left col., l. 7 to 10 of Stagljar :"The WBP1-Cub-PLV fusion gene was generated by site-directed integration of a PLV cassette containing the 5'- truncated Δwbp1 gene (Δwbp1-Cub-PLV) into the genomic WBP1 locus"), a person of ordinary skill in the art would in my opinion expect that the genomic WBP1 locus would express WBP1 that was not tagged in any form. The person of ordinary skill in the art would also expect that the episomally maintained pRS305 plasmid, assumed for this discussion that the plasmid does not contain a 5'-truncated Δwbp1 gene (which would not be functional when episomally expressed), but a complete wbp1 gene, would in addition express the Cub-PV tagged WBP1. Thus, it is my opinion that the person of ordinary skill in the art would

expect two types of Wbp1 protein to be present in the cell, one that is tagged with Cub-PLV (expressed by the episomally maintained plasmid) and one Wbp1 that is not tagged (expressed by the genomic WBP1 locus).

In my opinion, the person of ordinary skill in the art would have, at the time the invention was made, expected the un-tagged genomic WBP1 protein and the episomally expressed Cub-PLV tagged WBP1 protein to compete for protein - protein interactions. Since only the interaction with the Cub-PLV tagged WBP1 protein could be detected, the un-tagged genomic WBP1 protein also present in the cell would be expected to interfere with the detection of protein-protein interactions and thus to compromise the sensitivity of Stagljar's assay.

This expected decrease in sensitivity could not be readily counteracted by expressing the Cub-PLV tagged WBP1 in relatively high amount. As stated in our paper ("Stagljar") on page 5191, right col., l. 9 to 11, unpublished data that we had gathered showed that "overexpression of WBP1-Cub-PLV . . . results in gene activation in the absence of Nub," thus putting the person of ordinary skill in the art on alert that an high expression of the Cub-PLV tagged WBP1 is not an option.

For the stated reasons, it is my opinion that the person skilled in the art would have been deterred from episomally maintaining pRS305.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of

Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Toronto,
July 20, 2010
Date:

Prof. Igor Stagljar, Ph.D.